

AGCAGAGAGCCTGGTGGCATGGACATCTTATCCACATACCTTAGTGTGAC
 CACGCCGACAGAAAACTACTAAGGCCATCTCAGGGTGCCTGTGCCAGGAGA
 GGGGGCGGTGCCCCGGGCCAGAGCCATGCCCTCGGCCTGAAGCTCCG
 CAGGACTCGGCCTACAACGTCTGAGCAAGAACTGCTTGTGCCGGATC
 CGCCTGCTGGACAGCAATGTCATCGAGTGCACGCTGTCGGTGGAAAGCACGG
 GGCAAGAGTGCTGGAGGCCGTGGCCCCAGAGGCTGGAGCTGAGGGAGACGC
 ACTACTCGGCCTTGGTTCTCAGCAAGAGCCAGCAGCGAGATGGGTAGA
 GCTGGAGAACGCCACTGAAGAAACATCTGGACAAGTTGCTAACGAGCCTCTG
 CTTCCTCGGAGTCATGTTCTATGTGCCAAATGTGTACGGCTTCAGCAGGA
 GCCACAAGATATCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGA
 CGGTTGCGGTGCTCCCTGGAACAAGTGTACCGGCTGGCTGGCTAGCTGTG
 AAGCTGACTTCGGAGATTATAACCAGTTGATTCCAAGAGTCCCTCCGAGA
 GTATGTGCTCTTCCTATGGATTGGCATGGAGGAGGCGGCTGGAGGAG
 CTAACCCAGAACGGTGGCCCAGGAACACAAAGCTCATAGCGGGATCCTGCCG
 GCTGAAGCTGAACGTACATCAACGAGGTAGAGCGTTGGATGGATTG
 GACAGGAGATCTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGG
 CATCTTCTCATGGGATTTGTGAGGAACAGGGTCGGAGACAGGCAGTG
 ATATACAGGTGGAATGACATTGGAGTGTACTCACAGCAAAGCAGCCATCC
 TGTTGGAGCTGATTGACAAGGAGGAGACCGCGCTTCCATACAGATGATAT
 TGAAAATGCCAAGTACATTCTGGTTGTTACCACTCGGCACAAATTACA
 AACAGAACAAAGATCTGCACTGAACAGTCAAATTCTCCACCCCCAATCAGACG
 CCAGCCCACCTGGAGCCGGTCCTCACTGCCAAGGCAGCAGCCGTATATCTG
 CCTCCCATGCATGTCCAGTGCAGTGACTACTCGGAGACCCATACTCCCA
 AGACAGCATTTCGGGAACGAAGAACGCTTGTACTGCCGTCTCACAAAC
 AGCCTGGACCTTAATTACTGAAACGGCACCGTCACCAATGGCAGCGTGTGCA
 GCGTTCACAGCGTCAACTCCCTCAGCTGCTCCAGAGCTTCATTCAAGCGTCT
 CCAGTGTCTCCAACCTAGCATCCCTGGAGTGCACATCATGAGGGCCGATT
 ACATCCCCAGCCACCGCCACAGCACCATCATGCGCTCTACAGGCCGAC
 CCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCTGATGCACGC
 AGACAGCCAGAGCCGGTCTCGCTAACCTCAATATCATCAACACCCATGCC
 TATAACCAGCCGAGGAACGGTACAGCCAGCCGGAGATGCCGGAGAGG
 CATCCCTACACGGTCCCTATGCACACCAGGGGTCTACGGTCACAAACTTG
 TAAGTCCGTCTGACCAGATGAACCCCCAAATTGTGCGATGCCATCAAGCC
 AGGGGCCAGTCCATCTCACACAGTGCAGCACTCCAGAACTAGCCAACATG
 CAGCTCCAAGGAGCACAACACTATAGCACAGCCCACATGCTCAAGAACTATC
 TATTCAAGGCCGCCACCCCTTACCCCTCGGCCGGTCTGCCACCAGCACCCCA
 GACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGATCTGG
 TAACTCGGAAGGTGCAGCTCTCGTAAAGACCTCCAGGAGGACAGCTCACC
 TGTGGTCCATCAGTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAG
 CACCATGGCGGCGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTG

FIGURE 1A

ATGAACAGCATGGT GAGAGGCATGGAGGCCATGACACTGAAGTCACTCAATA
 TCCCCATGGCTCGCCGCAACACCCCTCGGGAGCAGGGCCCTCCGAGGAGAC
 GGGCGGCCACGAAGTGCACGGTCTCCCCAGTATCACCAAGAACAGACATT
 TCGGATGCCACCAGTGTGATCCACAGCAGTGAGAGCGAGGAAGAGGAGGAG
 ACCCTGGAGGCTGCACCTCAGGTTCTGTGCTTGAGAGAAAGTAGAATACA
 GTGCCCAGCTGCAGGCTGCCCTGGCCCGATCCCCAACAGGCCCCACCTGA
 GTACCCAGGGCCAAGAAAAAGTGTCAAGTAATGGGGCACTGAGACAGGACCA
 GGGAACCCCTCTCCTGCCATGCCAGGTGCAGGGTGCTGAGACACGGACCA
 TCCAAGGCCCTCAGTGTCTCCCGGGCAGAGCAGCTGGCTGTCAACGGTGCCT
 CTCTGGGTCCCTCCATCTGAGCCTGACCTAACCAAGCGTGAAGGAGCAGGGT
 CAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTCAAGAGATGTTCTCCCTGGAG
 GACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAACAGAACAG
 ATGACGGGCCCGCAGGCACAGAACAGAGACCGCTGATGTTGGCAGCGCTGAAT
 GGGCTCTCGGTGGCCCGAGTGTGCGGGGGAGATGGTCGCCATGATGCCA
 CCCGAGTCCCCATAGACGAGAGGCTCAGAGCCCTGAAGAACAGCTGGAAAG
 ATGGAATGGTGTTCACAGAATATGAGCAGATTCAAACAAAAAGGCCAACG
 GCGTCTCAGCACCGCCACTCTGCCTGAGAACGCCAGCGCAGCCGGATCCG
 AGAAGTTGTCCCATTAGAGGAGAACATCGAGTGGAGCTCATCCGACCAAAGAA
 AACAAACACAGGCTATATCAACGCCCTCACATCAAGGTGGTGGCGCGGAT
 CAGAATGGCACTACATGCCACCCAGGGGCCCTGCCACATACGTGCCATGA
 CTTCTGGCAGATGGTGTGGAGCAGGGGGTGAATGTGATGCCATGGTCACT
 GCAGAGGAGGAGGGTGGACGGACAAAAGCCATCGATACTGGCCCAAACGT
 GGGTCCAAGCATAGTTCTGCCACCTACGGCAAGTTCAAGGTACCACAAAGT
 TCCGGACAGATTCTGGTGCTATGCAACGACGGCCTAAAGGTGAAGCACCT
 GCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTACACGGACTGGCCC
 CACCACGGCTGTCCAGAACAGCTCCAAGGATTGGTCTACTTGGAGGAAA
 TCCAGTCAGTCCGACGCCACACCAACAGCGTGTGGAAAGGCATCAGGACCAAG
 GCACCCCCCCCATCGTGGTCACTGCAGCGCGGGTGTGGAAAGGACTGGTGTG
 GTTATCCTCTGTGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGG
 AGGTGCCACGATGCTGCGATTCTCAGGGAGCAGAGGATGTTCATGATCCA
 GACCATTGCGCAGTACAAGTTGTCTACCAAGTCCTCGCCAGTCCCTGCAGA
 ATTCCAGGCTCATTGATCTCCTCCGGGATGCGAGCTCTGGAGGAGGGACGC
 AGCTCTGCTCGCAGGGGGCGGCCACTCGACAAACATCTGCCTCCCCAGCC
 AGAGGGTGGATGGCTGGCAGCAGGAGAACGCCAGAGTTACTCACAAACATCA
 TGTATTATTTATATAAGATAATITATTGGTCTCTTGGAAATAAGTCTG
 TGAGTTATTATATAATGCTCCCCCCCACACACACACAATAATAGTGCT
 TCTCATTG (SEQ ID NO:1)

FIGURE 1B

underlined = deleted in targeting construct

bold = sequence flanking Neo insert in targeting construct

AGCAGAGAGCCTGGTGGGCATGGACATCTTATCCACATACCTTAGTGTGACCACGCCGA
CAGAAAACTACTAAGGCCATCTCAGGGTGCCCTGTGCCAGGAGAGGGGGCGGTGTCCCC
GGGCCGCAGAGCCATGCCCTTCGGCCTGAAGCTCCGCAGGACTCGGCCTACAACGTCT
GAGCAAGAACTGCTTGTGCCGGATCCGCCTGCTGGACAGCAATGTCATCGAGTGCAC
GCTGTCGGTGGAAAGCACGGGCAAGAGTGCCTGGAGGCCAGAGGCTGGAGCT
GAGGGAGACGCACTACTTCGGCCTTGGTTCTCAGCAAGAGCCAGAGCGAGATGGGT
AGAGCTGGAGAACGCCACTGAAGAACATCTGGACAAGTTGCTAACGAGCCTCTGCTTT
CTTCGGAGTCATGTTCTATGTGCCAAATGTGTCACGGCTTCAGCAGGAGGCCAACAGATA
TCAGTATTACCTGCAAGTCAAAAAGACGTGCTGAAGGACGGTTGCAGGCTCCCTGGA
ACAAGTGATCCGGCTGGCTGGCTTAGCTGTGCAAGCTGACTTCGGAGATTATAACCAGTT
TGATTCCCAAGAGTTCCTCCGAGAGTATGTGCTCTTCCTATGGATTGGCCATGGAGGA
GGCGGCTCTGGAGGAGCTAACCCAGAACAGGTTGGCCCAGGAACACAAAGCTCATAGGGGAT
CCTGCCGGCTGAAGCTGAACGTGATGTACATCAACGAGGTAGAGCGTTGGATGGATTGG
ACAGGAGATCTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGGCATTTCTT
CATGGGGATTTGTGAGGAACAGGGTCGGGAGACAGGCAGTGATATACAGGTGGAATGA
CATTGGGAGTGTACTCACAGCAAAGCAGGCCATCCTGTTGGAGCTGATTGACAAGGAGGA
GACCGCGCTTCCATACAGATGATATTGAAAATGCCAAGTACATTCTGGTTGTTAC
CACTCGGCACAAATTAAACAGAACAGATCTGCACTGAACAGTCAAATTCTCCACC
CCAATCAGACGCCAGCCCACCTGGAGCCGGTCTCACTGCCAAGGCAGCAGCCGTATAT
CTTGCCCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCAAGA
CAGCATTTCAGGGAACGAAGAACGCTTGTACTGCCGTTCTCACAAACAGCCTGGACCT
TAATTACTTGAAACGGCACCGTCACCAATGGCAGCGTGTGCAGCGTTCACAGCGTCAACTC
CCTCAGCTGCTCCAGAGCTTCATTCAAGCGTCTCCAGTGTCTCCAACTTAGCATCCC
TGGGAGTGAACATCATGAGGGCCGATTACATCCCCAGCCACCGCCACAGCACCATCATG
GCCGTTACAGGCCACCCCCAGATTACGAGACGGTCATGAGGAGATGAAGAGGGTCT
GATGCAGCAGACAGCCAGAGCCGGTCTCGCTAACCTCAATATCATCAACACCATGC
CTATAACCAGCCGAGGAACCTGGTGTACAGCCAGCCGGAGATGCCGGAGAGGCATCCCTA
CACGGTCCCCATGCACACCAGGGTGCTACGGTCACAAACTTGTAAAGTCCGTCTGACCA
GATGAACCCCCAAATTGTGCGATGCCATCAAGCCAGGGCCAGTTCCATCTCACAC
AGTGAGCACTCCAGAACATGCCAGCTCCAGGAGCACAAACACTATAGCACAGC
CCACATGCTCAAGAACTATCTATTCAAGGCCACCCCCCTAACCTCGGCCGCTCTGC
CACCAGCACCCAGACCTGCCAGGCCACCGCCACAGTACGTCAGCGGCAGCAGCCCTGA
TCTGGTAACCTCGGAAGGTGCAGCTCCGTAAAGACCTCCAGGAGGACAGCTCACCTGT
GGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAGCACCATGGCGG
CGGCGGTGGCACGGTGAATAACGCCACAGCCTGGAGGTGATGAACAGCATGGTGAGAGG
CATGGAGGCCATGACACTGAAGTCACTCAATATCCCCATGGCTGCCGCAACACCTTCG
GGAGCAGGGCCCTCCGAGGAGACGGCGGCCACGAAGTGCACGGTCTCCCCAGTATCA
CCACAAGAAGACATTCTCGGATGCCACCATGCTGATCCACAGCAGTGAAGAGCGAGGAAGA

FIGURE 2A

GGAGGAGACCCTGGAGGCTGCACCTCAGGTTCTGTGCTCGAGAGAGAAAGTAGAATACAG
TGCCCAGCTGCAGGCTGCCCTGGCCCGATCCCCAACAGGCCACCTGAGTACCCAGG
GCCAAGAAAAAGTGTCACTGAGACAGGACCAGGGAACCCCTTCCCTGC
CATGGCCAGGTGCAGGGTGCAGACACGGACCCTCAAGGCCCTCAGTGTCTCCGGGC
AGAGCAGCTGGCTGTCAACGGTGCCTCTGGTCCCATCTGAGCCTGACACTAAC
CAGCGTAAGGAGCGGGTCAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGCAGAGATGTT
CTCCCTGGAGGACAGCATTATAGAGAGAGATGATGATCAGGAATCTAGAGAACAGAA
GATGACGGGCCCGCAGGCACAGAACAGAGACCGCTGATGTTGGCAGCGCTGAATGGCTCTC
GGTGGCCCGAGTGTGGGGGGAGATGGTCGCCATGATGCCACCCAGTCCCCATAGA
CGAGAGGCTCAGAGCCTGAAGAACAGCTGGAAGAGATGGAATGGTGTACAGAACATGA
GCAGATTCCAACAAAAGGCCAACGGCGTCTCAGCACCGCCACTCTGCCGTGAGAACGC
CGAGCGCAGCCGGATCCGAGAACAGTTGTCCCATATGAGGAGAACAGTGGAGCTCATCCC
GACCAAAGAAAACAACACAGGCTATATCAACGCCTCCACATCAAGGTGGTGGTCCGG
ATCAGAAATGGCACTACATCGCCACCCAGGGCCCTTGCACATACGTGCCATGACTTCTG
GCAGATGGTGTGGAGCAGGGGTGAATGTGATGCCATGGTCACTGCAGAGGAGGAGGG
TGGACGGACCAAAAGCCATCGATACTGGCCAAACTGGGTCCAAGCATAGTTCTGCCAC
CTACGGCAAGTTCAAGGTACCACAAAGTTCCGGACAGATTCTGGTGTATGCAACGAC
GGGCCTAAAGGTGAAGCACCTGCTGCCGGCAGGAGAGGACCGTGTGGCACTTGCAGTA
CACGGACTGGCCCCACCACGGCTGTCCAGAACAGACGTCAAGGATTTTGTCCTACTTGG
GGAAATCCAGTCAGTCCGACGCCACACCAACAGCGTGTGGAAAGGCATCAGGACCAGGCA
CCCCCCCCTCGTGGTCACTGCAGCGGGTGTGGAAAGGACTGGTGTGGTTATCCTCTC
TGAGCTCATGATCTACTGCCTGGAACACAACAGAAAAGGTGGAGGTGCCACGATGCTGCG
ATTCCCTAGGGAGCAGAGGATGTTCATGATCCAGACCATTGCGCAGTACAAGTTCGTCTA
CCAAGTCCTCGTCCAGTTCTGCAGAATTCCAGGCTCATTTGATCTCCTCCGGGATGCAG
CTTCTGGAGGAGGGACGCAGCTCTGCCTGCAGGGGGCGGCCACTCGACAACATCTGCC
TCCCCCAGCCAGAGGTGGATGGCTGGCAGCAGGCAGAACGCCAGAGTTACTCACAAACATC
ATGTATTATTTATATAAGATAATTATTTTCCCTTTGGAATAAGTTCTGTGAGT
TATTATATAATGCTTCCCCCCCATAACACACACACAATAATAGTGTCTCATTG

FIGURE 2B

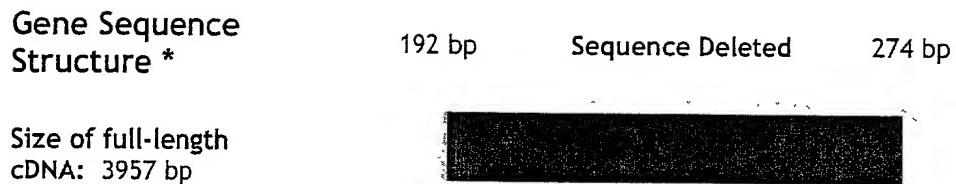


FIGURE 3

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Targeting Vector*
(genomic sequence)

Arm Length:
5': 3.5 kb
3': 2 kb

Targeting Vector
- - - Endogenous Locus

* Not drawn to scale

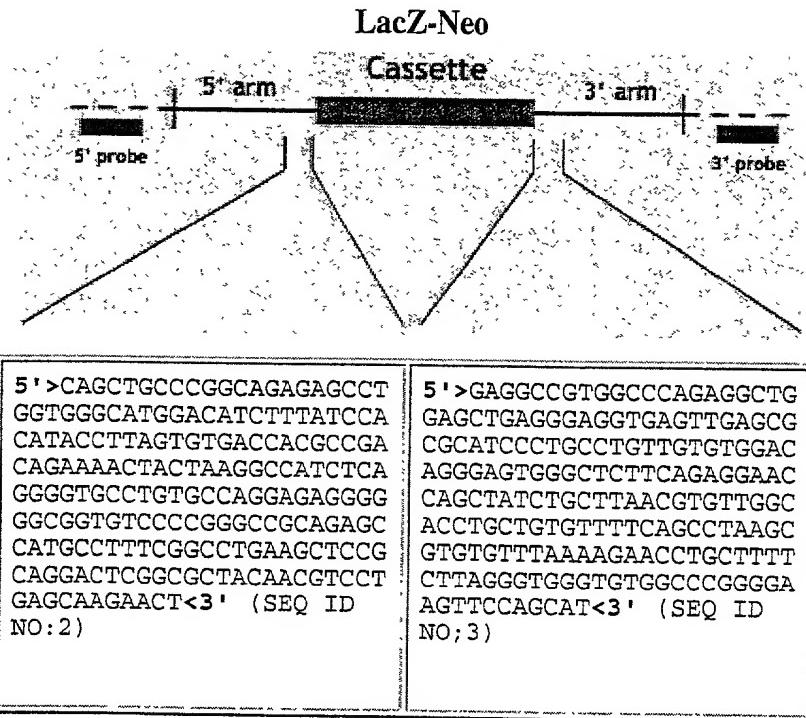


FIGURE 4